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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/027,671	02/23/1998	ALAN K. SMITH	4292-0048-55	3507

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EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
027,671	SMITH et al
Examiner	**Group Art Unit**
SAUNDERS	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 6/5/02.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 6-12, 38-45, 47-48 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 6-12, 38-45, 47-48 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 27

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

The amendment of 6/5/02 (Paper 26) has been entered.

Claims 6-12, 38-45 and 47-48 are pending and under examination.

Applicant is reminded that page 19 of the specification contains an improper reference to an attorney docket number.

Claims 9 and 43 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In claim 9 "Periodically or continuously" recite all possible embodiments.

In claim 43 "hematopoietic progenitor cells" is inconsistent with claim 38.

The amendment of 6/5/02 has overcome previously stated rejections under 35 U.S.C. 112.

Claims 7-12, 38-45 and 47-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claims require one to obtain lineage committed human cells which are "more differentiated than human stem and progenitor cells". The disclosure at pages 6-7 sets forth no clear line of demarcation between progenitor cells, lineage committed cells and mature cells. Note especially the contrasting embodiments set forth at page 7, lines 5-7. While the art might have reasonably identified the various stages from hematopoietic stem cell to mature

hematopoietic cell and have sufficiently established nomenclature for these stages, it is not clear how these terms would apply to other pathways of differentiation (e.g. to neural, kidney tissues) where the stages of differentiation have not been well characterized. Since the lines that demarc a "lineage committed human cell" from a progenitor cell or differentiated cell are fuzzy one has no idea of the metes and bounds of what is claimed.

Claims 7-12, 38-45 and 47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for obtaining lineage committed cells that are hematopoietic cells (e.g. as listed at page 7, lines 14-18) or B/T cells (as listed at page 7, lines 20-22), does not reasonably provide enablement for obtaining any and all of the types of lineage committed cells listed in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Applicant's disclosure has not enabled the practice of the claimed invention for its full scope.

Of the cells exemplified, only the T-cells of Examples 1 and 2 have been shown by applicant to have enhanced biological function (e.g. secretion of lymphokines or growth factors). The chondrocytes of Example 3 merely showed enhanced replicative potential (expansion); applicant showed no enhanced biological function of these cells (as required by the claims) compared to statically grown chondrocytes. The examples given of obtaining T-cells are insufficient to support the breadth of the claimed invention.

As to types of cells other than hematopoietic cells or B/T cells it is not routine to obtain proliferating lineage committed cells (other than fibroblasts) from such sources as neural, pancreatic, muscle, or heart tissues. Applicant has pointed to no teachings/references of the prior art that would have directed one as to how to obtain such lineage committed cells from such diverse sources of particular tissues.

While various lineage committed cells were known that would form the types of hematopoietic cells disclosed at page 7, lines 14-18, it is not even known in the art what types of lineage committed cells are involved in the formation of other differentiated tissues such as neural, pancreatic, muscle, or heart, and it is not known how to identify such lineage committed cells if they exist.

Given the lack of knowledge by those skilled in the art as to how to find the appropriate stem cells and how to induce these upon the vast number of various routes of lineage commitment toward the vast array of kinds of differentiated tissues in the human encompassed by applicant's claims, applicant is claiming an invention which would require undue experimentation for one to conduct in its full breadth.

While an applicant may be entitled to claim generically, in this case there is little enabling disclosure, but for a limited number of examples which show obtaining hematopoietic lineage committed cells (T-cells), and these results cannot readily be extrapolated to obtaining lineage committed cells that would form other types of differentiate tissue. These examples

represent inadequate support to claim obtaining all types of lineage committed cells, and applicant is therefore not entitled to claim obtaining all.

Claims 8-12, 38-40, 42-43 and 47-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Emerson et al. (5,437,994) for reasons of record and as explained below.

Applicant has traversed the rejection on the grounds that Emerson et al. teach culturing of progenitor cells and not lineage committed cells. The examiner finds this argument unconvincing for the following reasons.'

1) Emerson et al. teach that stromal cells are present and show enhanced biological function (col. 7, lines 60-63, for example). Stromal cells are clearly within the scope of lineage committed cells (e.g. claim 43).

2) The cultures of Emerson et al. that underwent a high rate of medium exchange produced granulocyte and macrophages (col. 19, line 43 - col. 20, line 9). These are "more differentiated than human stem and progenitor cells" as required by instant claim 38.

3) Emerson et al. are culturing with medium exchange rates and with the use of other culture conditions (e.g. addition of growth/differentiation factors) indistinguishable from what applicant's have instantly disclosed. Even if they had not taught (as noted supra) the existence of lineage committed cells (such as stromal cells, macrophage, granulocyte), it is reasonable to consider that lineage committed cells would have been present, since Emerson et al. provided what applicant has disclosed as the conditions of culturing that are essential for obtaining lineage committed cells with enhanced biological function. See Ex parte Novitski 26 USPQ2d 1389.

Applicant is thus wishing to obtain a patent for something that was inherently accomplished in the method of the prior art.

New claim 48 has been added to the rejected claims because Emerson et al. teach continuous replacement of culture fluid (col. 5, line 68).

Claims 6, 9-12, 38-39, 41-42, 44, 46 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Freedman et al. (Jour. Immunol.. Meth 167,145, 1994) for reasons of record.

Applicant has traversed the rejection on the ground that "enhanced replicative potential" is not equivalent to expansion of cell numbers. Applicant then quotes page 9 lines 15-19 of the specification to show what "enhanced replicative potential" means. Applicant then states that this means that after culturing, the cells are capable of enhanced replication, for example, after transplantation to a patient. The examiner does not find any teaching at specification page 9, that the term "enhanced replicative potential" applies to the cells after their culturing or to any characteristic of the cells upon their transplantation to a patient; applicant is thus arguing an undisclosed limitation upon the term "enhanced replicative potential". The examiner has properly rejected the claims, since he has considered the reasonably broadest interpretation that can be given to this term as set forth in the disclosure.

Applicant has also argued that the enhanced biological function of preferential killing of autologous tumors cells was not due to enhancement but "due to the disappearance or significant reduction of the nonspecific cytotoxicity during the fourth step of the expansion." This argument is unconvincing of distinction from the prior art, because the paragraph spanning instant

specification pages 11-12 indicates that biological function is determined as an average property of the cell population as a whole. If the nonspecific cytotoxic cells did indeed disappear during the culturing disclosed by Freedman et al, then this biological function, determined as an average property of the resulting cell population as a whole would have been enhanced, in accord with applicant's claims read in light of the specification.

Applicant's urgings of 6/5/02 have been considered but are unconvincing.

Claims 8-10, 12, 38, 42-43 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Caldwell et al. (Jour. Cell Physiol, 147,344, 1991, ref. GY).

Caldwell et al. teach that increasing the medium exchange rate from 3.5X/week to 7X/week leads to a transient increase in biological function (secretion of GM-CSF) by cultured human bone marrow stromal cells. See abstract and pages 350-35. Claims 8-10, 38, 42-43 are thus anticipated.

Regarding claims 12 and 46, note that Fig. 4 shows enhanced proliferation of the cells in cultures having medium exchanged 7X/week.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D., whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday from 8:00 a.m. to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

D. Saunders:jmr

October 15, 2002

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644